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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/667,947	09/22/2000	Stephen James Russell	07039-298001	9619
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EXAMINER CHEN, SHIN LIN				
ART UNIT 1632 PAPER NUMBER				

DATE MAILED: 03/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/667,947

Applicant(s)

RUSSELL ET AL.

Examiner

Shin-Lin Chen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 February 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 27-37,43 and 45-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27-37,43 and 45-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Upon further consideration of the present invention, the finality of the Official action mailed 1-6-04 has been withdrawn.

Applicants' amendment filed 2-20-04 has been entered. Claims 1-26, 38-42, 44, and 54-58 have been canceled. Claims 27, 37, 43 and 45-53 have been amended. Claims 27-37, 43 and 45-53 are pending and under consideration.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 27-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14 and 17-21 of U.S. Patent No. 6,632,800 ('800). Although the conflicting claims are not identical, they are not patentably distinct from each other because, although drawn to different scope, they encompass the same invention and obvious variants thereof.

Claims 27-32 of the present invention are directed to a method of monitoring gene expression of virally encoded nucleic acid from virus infected cells comprising administering a

measles virus, comprising a nucleic acid sequence encoding a heterologous polypeptide, to an organism, wherein said nucleic acid is upstream of a nucleic acid encoding a viral polypeptide and said heterologous polypeptide is released into a biological fluid of said organism, and detecting the amount of said heterologous polypeptide is an indication of the amount of said gene expression. Claims 28 and 29 specify the heterologous polypeptide is biologically inactive and below 10 kDa, respectively. Claims 30-32 specify the heterologous polypeptide is a tumor antigen, a CEA, and a beta subunit of human chorionic gonadotrophin, respectively.

Claims 14 and 17-21 of '800 are directed to a method of monitoring the expression of a transgene in a patient comprising introducing a nucleic acid construct comprising a transgene and a sequence encoding a marker polypeptide under the control of a first and second promoters to said patient, respectively, wherein said marker polypeptide is released into an extracellular body fluid of said patient, and detecting the presence of said marker polypeptide as an indication that said transgene is expressed in said patient. Claims 17-19 specify the marker polypeptide is a beta-human chorionic gonadotrophin, a tumor antigen, and a CEA, respectively. Claims 20 and 21 specify the introduction step comprises administering a virus, such as measles virus, containing the nucleic acid construct to said patient.

The promoter taught by '800 could be an endogenous promoter of measles virus genome and the marker polypeptide as taught by '800 is considered a heterologous polypeptide. Further, the tumor antigen, CEA, and the beta subunit of human chorionic gonadotrophin all can be below 10 kDa. Thus, it would have been obvious for one of ordinary skill in the art at the time of the invention to practice the claimed invention of the present application according to the teachings of '800.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 27-37, 43 and 45-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "said nucleic acid sequence is upstream of a nucleic acid encoding a viral polypeptide" in claims 27 and 43 is vague and renders the claims indefinite. It is unclear whether the nucleic acid sequence is under the control of an endogenous viral promoter or a heterologous promoter, or there is no promoter sequence to direct the expression of said nucleic acid sequence. Claims 28-37 depend on claim 27 and claims 45-53 depend on claim 43. Claims 28-37 and 45-53 fail to clarify the indefiniteness.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(c), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 34-37, 43 and 45-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Russell et al., 2003 (US Patent 6,632,800).

Claims 27-37, 43 and 45-53 are directed to a method of monitoring gene expression of virally encoded nucleic acid from virus infected cells comprising administering a measles virus, comprising a nucleic acid sequence encoding a heterologous polypeptide, to an organism, wherein said nucleic acid sequence is upstream of a nucleic acid encoding a viral polypeptide and said heterologous polypeptide is released into a biological fluid of said organism, and detecting the amount of said heterologous polypeptide is an indication of the amount of said gene expression, and said measles virus used for said method. Claims 28, 29 and 45 specify the heterologous polypeptide is biologically inactive and/or below 10 kDa. Claims 30-32 and 46-48 specify the heterologous polypeptide is a tumor antigen, a CEA, or a beta subunit of human chorionic gonadotrophin. Claims 33, 34, 49 and 50 specify the nucleic acid sequence encodes a fusion protein comprising said heterologous polypeptide fused to an endogenous polypeptide, such as H protein. Claims 35, 36, 51 and 52 specify the fusion protein contains an amino acid linker sequence having a protease cleavage site, such as furin cleavage site. Claims 37 and 53 specify the measles virus is replication-competent.

Russell teaches a method of monitoring the expression of a transgene in a patient comprising introducing a measles virus containing a nucleic acid construct comprising a transgene and a sequence encoding a marker polypeptide, such as a beta-human chorionic

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gonadotrophin, a tumor antigen, or a CEA, under the control of a first and second promoters to said patient, wherein said marker polypeptide is released into an extracellular body fluid of said patient, and detecting the presence of said marker polypeptide as an indication that said transgene is expressed in said patient (e.g. abstract, column 31). Russell also teaches generation of an expression vector containing nucleic acids encoding 33 amino acid insulin C-peptide linked to nucleic acid encoding C-terminus of Measles H glycoprotein via furin-cleavable linkers so as to provide a chimeric H glycoprotein comprising C-peptide and H glycoprotein linked by furin-cleavage site (e.g. Example 1, 7). Russell further teaches introducing the expression vector into a full-length measles virus genome to produce a recombinant measles virus expressing a fusion protein comprising C-peptide and H glycoprotein linked by furin-cleavage site, and C-peptide can be used as a marker for the expression of a cell-associated transgene in vivo (e.g. Example 7, 8).

It would have been obvious for one of ordinary skill in the art at the time of the invention to generate the claimed measles virus and the method of using said measles virus to monitor gene expression of virally encoded nucleic acid from virus infected cells because Russell teaches introducing an expression vector expressing chimeric H glycoprotein into a full-length measles virus genome to produce a recombinant measles virus and the expression of the chimeric H glycoprotein would be under the control of viral promoter. Further, the insulin C-peptide is below 10 Kda, and the tumor antigen, CEA, and the beta subunit of human chorionic gonadotrophin all can be below 10 kDa.

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One ordinary skill in the art at the time the invention was made would have been motivated to do so in order to use C-peptide as a marker for the expression of a cell-associated transgene in vivo as taught by Russell with reasonable expectation of success.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.



**SHIN-LIN CHEN
PRIMARY EXAMINER**